ORIGINAL ARTICLE

Gut and Liver, Vol. 1, No. 1, June 2007, pp. 63-67

Analysis of the Effects of Stent Insertion and the Factors Related to Stent Retrieval in Chronic Pancreatitis Accompanying Main Pancreatic Duct Obstruction

Chang Hoon Kim, Seungmin Bang, Kyung Ho Song, Jeong Youp Park, Tae Joo Jeon, Sung Pil Hong, Jae Bock Chung, Seung Woo Park, and Si Young Song

Division of Gastroenterology, Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, Korea

Background/Aims: Obstruction of the main pancreatic duct (MPD) has been considered one of the major causes for pain in chronic pancreatitis (CP). In this study, we evaluated the efficacy of MPD stenting in painful CP, and tried to determine a guideline for stent removal. **Methods:** Sixteen patients with painful CP who underwent MPD stenting were included. Follow up ERCP was performed 3 months after stenting in all patients. Stents were removed in patients who achieved pain relief, complete stone clearance, and decreased MPD diameter after 3 months. **Results:** Before stenting, ERCP showed MPD stricture in 11 cases, MPD dilatation by stone in 1 case, concomitant stricture and stone in 4 cases. After stenting, complete pain relief was achieved in 13 patients (81.3%) and partial pain relief was achieved in 3 patient (18.7%). There was no patient whose pain was not relieved. Stents were removed in 7 patients who achieved pain relief, complete stone clearance, and decreased MPD diameter after 3 months. Decrease of MPD diameter was significantly greater in patient who could remove stent than those who could not (72.9% vs. 127.9% of initial MPD diameter, p=0.008). **Conclusions:** If partial or full pain relief is achieved after MPD stenting and follow up ERCP after 3 months shows decreased MPD diameter compared to the initial one, stent removal might be considered. **(Gut and Liver 2007;1:63-67)**

Key Words: Chronic pancreatitis; Pancreatic duct; Stricture; Stent

INTRODUCTION

The cause and course of pain, which is the main symptom in chronic pancreatitis (CP), is diverse and the pathogenesis of pain has not been elucidated.[1,2] Hence, a standardized therapy for pain is not available, and also it is difficult to evaluate the effectiveness of therapy. Therefore, treatment in painful CP has to be decided individually by cause, frequency, and severity of pain. Obstruction of the main pancreatic duct (MPD) by a stricture or stone is one of major causes for pain in CP, and endoscopic MPD stenting has been used widely as a less-invasive alternative to conventional surgery for the treatment of pain in CP.[3,4] Although most studies reported good short-term and mid-term outcome after stenting, the appropriate duration of stent placement, the optimal interval for exchanging stent and criteria for stent removal has not been clerarly defined.[4-10] The aim of present study were to evaluate the therapeutic effectiveness of MPD stenting and to analyze factors that might become clinical criteria for stent removal.

MATERIALS AND METHODS

1. Subjects

Between January 1999 and July 2006, 19 patients treated with MPD stenting due to painful CP and those who underwent follow-up endoscopic retrograde cholangiopancreatography (ERCP) after 3 months were identified in the Severance Hospital. Three patients who underwent

Correspondence to: Seungmin Bang
Division of Gastroenterology, Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, 134, Sinchon-dong, Seodaemun-gu, Seoul 120-752, Korea
Tel: +82-2-2228-1995, Fax: +82-2-393-6884, E-mail: bang7028@yumc.yonsei.ac.kr
Received on April 5, 2007. Accepted on May 11, 2007.

MPD stenting were excluded due to accompanying pseudocyst. To evaluate the efficacy of MPD stenting and analyze the factors related to the stent removal, we retrospectively assessed clinical variables such as age, gender, the cause of chronic pancreatitis, the finding of ERCP at stent insertion and removal, the location of lesion, the results of pancreatic duct stone retrieval as well as the presence or absence of pancreatic duct stone, the diameter of the inserted stent, the change of the MPD diameter after stenting and duration of stent placement. The maximal MPD diameter was measured, with corrections made for magnification by multiplying the measured duct diameter by the known endoscopic diameter divided by the endoscope diameter measured on the ERCP film. In addition, the ratio of MPD diameter after stenting for initial one was obtained.

2. Stenting technique

ERCP (TJF-200, 240 Olympus Co., Tokyo, Japan) was performed under conscious sedation. After traversing the dominant pancreatic duct stricture or the pancreatic duct stone with a hydrophilic guidewire, a pancreatic sphincterotomy was performed, and a 5-7 Fr plastic pancreatic stent or an 8.5-12 Fr plastic stent for biliary drainage was placed. For the cases with pancreatic duct stone, extracorporeal shock wave lithotripsy (ESWL) for stone fragmentation and endoscopic retrieval of pancreatic duct stone were attempted first, and then subsequently, stents were placed.

3. Evaluation of the effectiveness of therapy after stenting

The effectiveness of therapy on pain after stenting was classified as follows; (i) complete pain relief: defined as withdrawal of analgesics, (ii) partial pain relief: defined as reduction of analgesics dose, and (iii) no improvement: defined as no change in analgesics dose.

4. Follow up ERCP and Criteria for stent removal

Follow up ERCP was performed 3 months after stenting in all patients. Stents were removed in patients who achieved pain relief, complete stone clearance, and decreased MPD diameter after 3 months.

5. Statistical analysis

For the evaluation of the efficacy and the analysis of factors related to stent removal after MPD stenting, t-test was used for the comparison of continuous variables, and chi-square test was used for the comparison of categorical variables. For statistical analysis, the SPSS Window 13 (SPSS, Inc, Chicago, IL, USA) was used and p value lower than 0.05 was considered to be statistically significant.

RESULTS

1. Demographic and clinical characteristics

Among 16 patients, 11 (68.8%) and 5 patients (31.2%) male and female, and the mean age was 42.1±17.0 years. The cause of CP was alcoholic and idiopathic in 8 cases each. According to the Cambridge classification, initial ERCP showed feature of severe CP in all patients including MPD stricture in 11 cases, MPD dilatation by stone in 1 case, concomitant stricture and stone in 4 cases. The location of stricture was head and neck in 9 cases, and body in 6 cases and tail in 1 case. Demographic and clinical characteristics are presented in Table 1.

2. Main pancreatic duct stenting and complications

In the presence of pancreatic stones, prior to main pancreatic duct stenting, the retrieval of pancreatic stones was attempted by ESWL and endoscopic retrieval. As the result, pancreatic duct stones were retrieved completely in 2 out of 5 cases. The median diameter of inserted stent was 7 Fr (5-12 Fr), and the median duration of stent placement was 3.2 monthes. Complications of ERCP and

Table 1. Demographic and Clinical Characteristics

	n (%)
Sex (male/female)	11/5
Age (years)*	42.1±17.0
Etiology	
Alcohol	8
Idiopathic	8
Initial ERCP finding	
Stricture	11 (68.8)
Stone	1 (6.2)
Stricture and stone	4 (25.0)
Location of lesions	
Head and neck	9 (56.3)
Body	6 (37.5)
Tail	1 (6.2)

*Mean±SD.

Table 2. Short-Term Outcome after Main Pancreatic Duct Stenting

	n (%)
Complete pain relief	13 (81.3)
Partial pain relief	3 (18.7)
No improvement	0 (0)

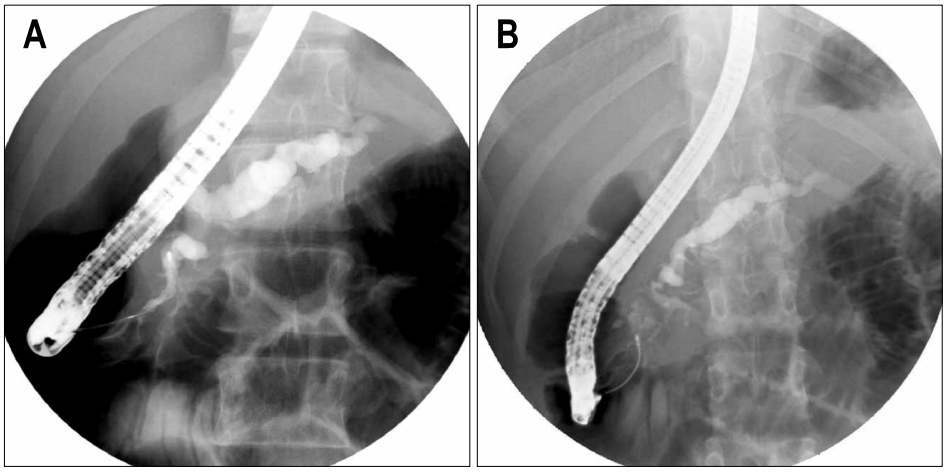

Fig. 1. ERCP finding after main pancreatic duct stenting. (A) Pancreatogram before main pancreatic duct stenting (MPD) shows severe chronic pancreatitis. (B) After 3 months, pancreatogram reveals a decreased maximal MPD diameter (93.2% of initial maximal MPD diameter).

MPD stenting included bleeding in 2 cases which was associated with pancreatic sphincterotomy and treated with electric coagulation. No other major complication occurred.

3. The short-term therapeutic effectiveness of MPD stenting

After stenting, complete pain relief was achieved in 13 patients (81.3%) and partial pain relief in 3 patient (18.7%). There was no patient whose pain was not relieved. (Table 2). The cause of CP, the location of lesion, the presence or absence of main pancreatic duct stricture, the presence of pancreatic stone and with or without its retrieval, the increase or decrease of the diameter of the MPD after stenting, and with or without stent removal showed no significant association with therapeutic effectiveness after MPD stenting.

4. Follow up ERCP and stent removal

In the follow up ERCP after 3 months, the maximal MPD diameter in the proximal area of stricture decreased in 9 cases (56.3%), increased in 6 cases (37.5%) and was unchanged in one case (6.2%). Among 9 patients who showed the decreased maximal MPD diameter after 3 months, stents were removed in 7 patients who achieved pain relief, complete stone clearance, and decreased MPD diameter after 3 months (Fig. 1).

5. Comparison between stent removed group and stent maintained group

Stents were removed in 7 patients (43.8%) and maintained in 9 patients (56.2%) after 3 months. Age, gender, the cause of chronic pancreatitis, the location of lesion, the presence or absence of MPD stricture, and the results of pancreatic duct stone retrieval as well as the presence or absence of pancreatic duct stone were not different between the two groups, but MPD diameter decrease was significantly greater in patient who could remove stent than those who could not (mean 72.9% *vs.* 127.9% of initial MPD diameter, p=0.008) (Table 3).

Table 3. Comparison between Stent Removed Group and Stent Maintained Group

	Stent removed group	Stent maintained group	p-value
Age (years)*	45.0±17.0	39.9±17.6	0.568
Sex			0.308
Male	6	5	
Female	1	4	
Etiology			1.000
Alcohol	4	4	
Idiopathic	3	5	
Lacation of lesions			0.126
Head and neck	2	7	
Body and tail	5	2	
Stricture			1.000
Present	7	8	
None	0	1	
Stone			0.308
Present	1	4	
None	6	5	
% of MPD†	72.9	127.9	0.008

*Mean±SD.
†Maximal MPD diameter is significantly greater in patient who could remove the stent compare to those who can not (mean 72.9% *vs.* 127.9% of initial MPD diameter, p=0.008).
MPD, main pancreatic duct.

6. The results of long-term follow up

The median follow up period from the day of stenting

to the last hostital visit of total 16 patients was 18.8 months (range, 6.40-59.7 months). Pain was well controlled in 6 patients of the stent removal group without additional stenting or surgery during median follow up period of 22.0 months (range 4.0-53.0 months). In 1 patient, pain recurred after 5.4 months, and eventually surgery (partial pancreatectomy and splenectomy) was performed. The mean number of the stent exchange was 2.8 times in the stent maintained group, and in 1 case, the stent was eventually removed under the condition of pain control, and pain did not recur. Among 16 patients, 2 patients (12.5%) were diagnosed as pancreatic cancer after 10.1 months and 57.5 months each.

DISCUSSION

Pain is one of the main symptoms of CP, and 60 to 70% of patients will develop pain during the course of the CP.[1] Although pain is multifactorial, the increase of pressure in the pancreatic duct and the pancreatic parenchyma due to the main pancreatic duct obstruction and inflammatory infiltration of pancreatic nerves are considered important factors.[2,11,12] In addition, complications of CP such as pseudocyst and bile duct obstruction have to be considered as the cause of pain. In chronic pancreatitis with such diverse etiologies of pain, it is very difficult to determine the leading cause of pain in each patient and to select the optimal therapy as well as to evaluate therapeutic effectiveness objectively.

Endoscopic MPD stenting has been introduced for the control of pain in CP in the late 1980s as a less-invasive alternative to conventional surgery.[3,13] The aim of MPD stenting is to relieve pain by ductal decompression and facilitate the secretion of pancreatic juice.[14] For these reasons, MPD stenting seems to be useful for patient with one dominant stricture in the pancreatic head and upstream ductal dilatation.[15,16] In previous studies, it has been reported that immediate pain relief was show in 74-94% after MPD stenting in CP with main pancreatic duct obstruction.[4,17,18] Nevertheless, most studies reported only short-term and mid-term therapeutic effectiveness after MPD stenting, and the long term therapeutic effectiveness of MPD stenting was doubtful. According to a large multicenter retrospective study presented recently in Europe, pain relief was maintained continuously in long-term follow up after MPD stenting.[5,19] In our study, complete or partial pain relief could be achieved in all 16 patients with MPD stenting, and a reason for such high effectiveness might be that all subjects had the findings of the distal obstruction and proximal dilatation of the MPD due to pancreatic duct structure and pancreatic stones prior to stenting, which suggested that the major cause of pain was the elevation of the pressure in the pancreatic duct in these patients.

Regarding the change of the MPD diameter after stenting, Binmoeller et al have reported that the MPD diameter was decreased a mean of 1.6 mm after stenting in 51 out of 58 patients (88%).[4] On the other hands, Morgan et al. have reported that the MPD diameter was increased a mean of 2.7 mm after stenting in 70% patients. Particularly, in the 77% of 26 patients who showed the improvement of pain after stenting, the MPD diameter was increased, and the MPD diameter was decreased in 23%. Thus, they concluded that the change of the MPD diameter after stenting was not a good indicator of pain relief.[20] In our study, like later study, the increase or decrease of the diameter of MPD after stenting was not associated with the therapeutic effectiveness on pain. Therefore, our data suggested increased intraductal pressure might be a cause for a pain, but ductal diameter was not associated with pain relief. More studies are needed to understand this contradicting result.

The appropriate duration of stent placement, the optimal interval for exchanging stent and the time of stent removal has not been clearly defined. The stent was exchanged in patients with recurrent pain or every 2-4 months as scheduled.[4-9] In addition, pain relief and disappearance of the proximal MPD dilatation have been suggested to be clinical criteria for stent removal.[5,10] In our study, stents were removed in patients who achieved pain relief, complete stone clearance, and decreased maximal MPD diameter after 3 months, but stents were exchanged, even if pain were improved, if pancreatic duct stones could not be retrieved or the maximal MPD diameter were increased or not changed. When we analyzed the clinical variables retrospectively, the maximal MPD diameter was decreased a mean 3.4 mm in patient who could remove stent. Also, MPD diameter decrease was significantly greater in patient who could remove stent than those who could not (mean 72.9% *vs.* 127.9% of initial MPD diameter, p=0.008). Therefore, although MPD diameter decrease was not a good indicator of therapeutic effectiveness, it might be considered as a factor related to stent removal after MPD stenting. To consider the stent removal or exchange by performing the follow up ERCP after 3 months was in agreement with the results of previous studies that the continuous placement of the stent was not associated with the pain control and severe complication like necrotizing pancreatitis or pancreatic abscess could be prevented by the scheduled stent exchange.[5,6]

This study is limited by a relatively small population,

retrospective analysis and lack of control groups. It is also possible that the therapeutic effectiveness on pain after MPD stenting may be contributed to the retrieval of pancreatic duct stone, pancreatic sphincterotomy and the natural course of CP.

In conclusion, MPD stenting is an effective therapy in CP for pain caused by the main pancreatic duct obstruction and if partial or full pain relief was achieved after MPD stenting and follow up ERCP showed decreased MPD diameter compared to the initial one after 3 months, stent removal might be considered.

REFERENCES

1. Jansen JB, Kuijpers JH, Zitman FJ, van Dongen R. Pain in chronic pancreatitis. Scand J Gastroenterol Suppl 1995; 212:117-125.
2. Di Sebastiano P, Friess H, Di Mola FF, Innocenti P, Buchler MW. Mechanisms of pain in chronic pancreatitis. Ann Ital Chir 2000;71:11-16.
3. Huibregtse K, Schneider B, Vrij AA, Tytgat GN. Endoscopic pancreatic drainage in chronic pancreatitis. Gastrointest Endosc 1988;34:9-15.
4. Binmoeller KF, Jue P, Seifert H, Nam WC, Izbicki J, Soehendra N. Endoscopic pancreatic stent drainage in chronic pancreatitis and a dominant stricture: long-term results. Endoscopy 1995;27:638-644.
5. Eleftheriadis N, Dinu F, Delhaye M, et al. Long-term outcome after pancreatic stenting in severe chronic pancreatitis. Endoscopy 2005:223-230.
6. Farnbacher MJ, Muhldorfer S, Wehler M, Fischer B, Hahn EG, Schneider HT. Interventional endoscopic therapy in chronic pancreatitis including temporary stenting: a definitive treatment? Scand J Gastroenterol 2006;41:111-117.
7. Vitale GC, Cothron K, Vitale EA, et al. Role of pancreatic duct stenting in the treatment of chronic pancreatitis. Surg Endosc 2004;18:1431-1434.
8. Topazian M, Aslanian H, Andersen D. Outcome following endoscopic stenting of pancreatic duct strictures in chronic pancreatitis. J Clin Gastroenterol 2005;39:908-911.
9. Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy 2003;35:553-558.
10. Bartoli E, Delcenserie R, Yzet T, et al. Endoscopic treatment of chronic pancreatitis. Gastroenterol Clin Biol 2005; 29:515-521.
11. Bradley EL 3rd. Pancreatic duct pressure in chronic pancreatitis. Am J Surg 1982;144:313-316.
12. Bockman DE, Buchler M, Malfertheiner P, Beger HG. Analysis of nerves in chronic pancreatitis. Gastroenterology 1988;94:1459-1469.
13. Kozarek RA, Patterson DJ, Ball TJ, Traverso LW. Endoscopic placement of pancreatic stents and drains in the management of pancreatitis. Ann Surg 1989;209:261-266.
14. Widdison AL, Alvarez C, Karanjia ND, Reber HA. Experimental evidence of beneficial effects of ductal decompression in chronic pancreatitis. Endoscopy 1991;23:151-154.
15. Neuhaus H. Pancreatic stents in chronic pancreatitis: do they function as a tube, a wick, or a placebo? Gastrointest Endosc 2006;63:67-70.
16. Neuhaus H. Therapeutic pancreatic endoscopy. Endoscopy 2004;36:8-16.
17. Cremer M, Deviere J, Delhaye M, Baize M, Vandermeeren A. Stenting in severe chronic pancreatitis: results of medium-term follow-up in seventy-six patients. Endoscopy 1991;23:171-176.
18. Lohr M, Schneider HT, Farnbacher M, et al. Interventional endoscopic therapy of chronic pancreatitis. Z Gastroenterol 1997;35:437-448.
19. Rosch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy 2002;34: 765-771.
20. Morgan DE, Smith JK, Hawkins K, Wilcox CM. Endoscopic stent therapy in advanced chronic pancreatitis: relationships between ductal changes, clinical response, and stent patency. Am J Gastroenterol 2003;98:821-826.